

#### Biosketch

John Kuriyan is currently Dean of Basic Sciences, School of Medicine, and Professor of Chemistry and Biochemistry at Vanderbilt University. He earned his PhD in 1986 from the Massachusetts Institute of Technology.

He was a post-doctoral fellow with Professors Martin Karplus (Harvard) and Gregory A. Petsko (MIT). From 1987 to 2001 he was on the faculty of The Rockefeller University, New York, and a Professor at the University of California Berkeley from 2002 until 2023. He was an HHMI investigator from 1990 until 2023.

### **Key Publications**

"Mechanism for activation of the EGF receptor catalytic domain by the juxtamembrane segment," 2009 *Cell* 137, 1293-1307. doi:10.1016/j.cell.2009.04.025

"Deconstruction of the Ras switching cycle through saturation mutagenesis," 2017 *eLife*, 6. doi:10.7554/eLife.27810

"Allosteric communication in DNA polymerase clamp loaders relies on a critical hydrogen-bonded junction," 2021 *eLife* 10:e66181 doi:10.7554/eLife.66181

## VANDERBILT School of Medicine Basic Sciences

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## "Signaling Proteins: Mechanism, Evolution, and Structure"

The Kuriyan lab studies the mechanisms, evolution, and structures of the molecular switches that carry out cellular signal transduction. We use biochemical, biophysical, structural and cell biological analyses to elucidate mechanisms, and also study how these mechanisms change with evolution. A major focus of the lab is to understand the allosteric communication that enables proteins to be exquisitely responsive to input signals. We use high-throughput mutational analysis to determine the sensitivity of these mechanisms to perturbations in order to determine the molecular principles governing regulation and specificity.

Breakthroughs from the lab have included the determination of the switching mechanisms of several tyrosine kinases, including Src, ZAP-70, Btk, and EGFR. We have also advanced the fundamental understanding of the regulation of several other signaling proteins, including the Ras activator SOS, and CaMKII. Our insights have helped understand how the misregulation of these enzymes is often coupled to cancer and immune diseases, and have implications for the development of kinase-targeted drugs.

The lab has also made fundamental discoveries related to the structural basis for high-speed DNA replication. We are currently applying high-throughput mutagenesis methods to these systems to understand the functioning of the AAA+ ATPases that form the core of the clamp-loader complexes.

